GeneCore Version 4.5
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OM protein   protein search, using sw model

Run one: October 26, 2001, 17:47:30 ; Search time 43.54 Seconds
(without alignments)
481.499 Million cell updates/sec

Perfect score: 1118
Sequence: 1 MARLRRLLRRLRRLRRRLRR...PKTVRGRVTEYKKLMET 211

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 412676 seqs, 606249988 residues

Post processing:
Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

total number of hits satisfying chosen parameters: 412676

Database :   A_Geneseq_0601.*

No.	Score	% Match	Query Length	DB Length	DB ID	Description
1	1118	100.0	211	21	AAB18645	Amino acid sequence
2	1118	100.0	211	22	AAB62817	Human fibroblast g
3	778.5	69.6	220	18	AAW11548	Amino acid sequenc
4	774.5	69.4	208	14	AAR27207	Glia activating fa
5	774.5	69.4	209	14	AAR27213	Glia activating fa
6	774.5	69.4	208	15	AAR56505	Glia activating fa
7	774.5	69.4	208	16	AAR80784	Glia activating fa
8	774.5	69.4	208	16	AAW70822	Fibroblast growth
9	774.5	69.4	208	18	AAW11547	Amino acid sequenc
10	774.5	69.4	208	19	AAW75719	Fibroblast growth
11	774.5	69.4	208	19	AAW58024	Fibroblast growth

SUMMARIES

							Description
12	774.5				208	21	AAB30299	Fibroblast growth
13	774.5				208	21	AAY87856	Human FGF-9 protei
14	774.5				208	21	AAY49418	FGF-9, SEQ ID No:1
15	774.5				208	21	AAY12341	Human fibroblast g
16	774.5				208	22	AAB61663	FGF-9 protein, Hom
17	774.5				208	22	AAS02290	Human fibroblast g
18	774.5				208	22	AAH50245	Human fibroblast g
19	769.5				208	22	AAH50710	Human fibroblast g
20	769.5				207	15	AAR56504	Glia activating fa
21	758.5				205	12	AAP57204	Glia activating fa
22	758.5				206	15	AAR56506	Glia activating fa
23	758.5				206	13	AAP42607	Glia activating fa
24	758.5				206	13	AAR27211	Glia activating fa
25	742				206	15	AAR27212	Glia activating fa
26	742				175	15	AAR56508	Glia activating fa
27	742				176	15	AAR56509	Glia activating fa
28	742				177	14	AAR27208	Glia activating fa
29	742				178	13	AAR27210	Glia activating fa
30	729				159	15	AAR56510	Glia activating fa
31	729				160	15	AAR56511	Glia activating fa
32	708.5				207	20	AAY05474	Human FGF-16 prote
33	708.5				207	21	AAY58429	Human FGF-16 prote
34	708.5				207	20	AAY05473	Rat FGF-16 protein
35	705.5				207	21	AAY58428	Rat fibroblast gro
36	691.5				198	20	AAY05475	Rat FGF-16 protein
37	691.5				198	21	AAY58432	Rat fibroblast gro
38	683				142	15	AAR56504	Glia activating fi
39	670				173	20	AAY05476	Rat FGF-16 protein
40	670				173	21	AAY58431	Rat truncated fibr
41	325				268	19	AAS5031	Fibroblast growth
42	324.5				266	21	AAY97887	Rat fibroblast gro
43	324.5				266	21	AAY47852	Human FGF-16 prote
44	324				266	21	AAY87878	Human FGF-5 protei
45	324.0				267	4	AAPH2464	Encoded by OkP 2.0

ALIGNMENTS

RESULT   1

AAB18645   AAB18645 standard; protein; 211 AA.

XX
AC   AAB18645;
XX
DT   22-JAN-2001 (first entry)
XX
DE   Amino acid sequence of human fibroblast growth factor (FGF)-20.
XX
PF   glia-derived neurotrophic factor; eye disease; neuronal disease;
PF   neurotrophic factor; anti-apoptotic factor; retinitis pigmentosa;
KW   macular degeneration; diabetic retinopathy; retinitis pigmentosa;
KW   inherited retinal degeneration; surgery-induced retinopathy;
KW   retinal detachment; photic retinopathy; toxic retinopathy;
KW   trauma-induced retinopathy; wet age related macular degeneration;
KW   ARMD; retinopathy; fibroblast growth factor 20; FGF-20.
OS   Homo sapiens.
XX
PN   WO200054813-A2.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000W0-US07052.
XX
PR   15-MAR-1999; 99US-0124460.
TF   06-JAN-2000; 2000US-0174984.
XX
PA   (CHIR) CHIRON CORP.
PA   (RP4C) UNIV CALIFORNIA.
XX
PI   Manning WC, Dwarki VJ, Rendahl K, Zhou S, McGee LH, Lau D;
PI   Flannery JG, Miller S, Wang F, Di Polo A;

DR   WPI; 2000-618062/59;
PR   N-PN; AAA76765.
XX
PI
PI   treating or preventing eye diseases or inhibiting neovascular disease
PI   of the eye, comprises intraocularly administering a gene delivery
PI   vector that directs expression of neurotrophic factors or
PI   anti-angiogenic factors -
XX
PS   Disclosure: Fig 29; 84pp; English.
XX
CC   The present sequence represents human fibroblast growth factor (FGF) 20.
CC   FGF 20 is expressed with a few amino acids of the N-terminal.
CC   Vectors of the invention are used for treating or preventing eye
CC   diseases or inhibiting neovascular disease of the eye. The gene
CC   delivery vector directs the expression of one or more neurotrophic
CC   factors, or anti-angiogenic factors, such that the disease of the eye
CC   is prevented or treated. The gene delivery vectors are useful for
CC   treating or preventing diseases of the eye such as macular degeneration,
CC   diabetic retinopathy, inhibited retinal degeneration such as retinitis
CC   pigmentosa, glaucoma, surgery-induced retinopathy, retinal detachment,
CC   photic retinopathy, age retinopathy or trauma induced retinopathy, and
CC   for inhibiting neovascular disease such as wet age related macular
CC   degeneration (AMD) or retinopathy of prematurity.
XX
SQ   Sequence: 211 AA;

Query Match   100.0%; Score 1118; DB 21; Length 211;
Best Local Similarity   100.0%; Pred. No.1.6e-111;
Matches   211; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 MAALAVSHLAILALGLMVAAVVGHLTLEFLAKNGAAT-AAGCGLAAQAAHL 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1 maalavsqtlailalglmvaavvghltlefliakrsaatsaaqpaaahl 60

Qy   61 RCLLRRGHLRFLPRSSGWTVGRRRQRFLQTRRWAHLEFLSWAVKVWKRSGHYKS 120
          ||||||||||||||||||||||||||||||||||||||||||||||||
Db   61 kallrrgylrftahtdlpasqtlftqqtfellqtrrsgvwaslrrgylry 120

Qy   121 MHRKLLTYSSLFLRQHLTBEICLLKHYTVALHKACHTRKCAK 180
          |||||||||||||||||||||||||||||||||||||||||||
Db   121 mhrkllfysslflrqhlts/sgvwasl/kyt/alhkacytrkcak 180

Qy   181 SKEHQKFTHFLPRSVPSRVPSEVEYKRLMYT 211
          |||||||||||||||||||||||||||||||
Db   181 sktqkthflprsvpsrvpseveyqrdllmyt 211

XX
DR   WPI; 2000-618062/59;
PN   Wo200107595-A2.
XX   Homo sapiens.
XS
KW   Alzheimer's disease; diabetic neuropathy; osteoporosis.
KW   achondroplasia; cerebral lesion, cerebral oedema, senile dementia,
KW   angiogenesis; bone repair; cartilage defects;
KW   cell growth proliferation; tumour; restenosis; psoriasis; human;
PD   AAW42017;
AC   AAW42017;
XX
ID   02 MAY 2001   (first entry)
DR   Human fibroblast growth factor-CX (FGF-CX) amino acid sequence.
XX
FN
PD   01-FEB-2001.
XX
PF   27-JUL-2000; 2000WO-US20405.

XX
PR   27-JUL-1999; 1999-0145899.
PR   31-JAN-2001; 2001WO-0145585.
PR   03-JUL-2000; 2000US-0609543.
XX
PA   (CURA-) CURAGEN CORP.
XX
PI   Jetters M., Shimkets RA., Prayaga SK., Boldog FL., Yang M., Burgess C;
PI   Fernandes E., Herrmann JL., Lichenstein H;
XX
XX
DR   WPI; 2001-194717/16;
DR   N-PN; AAW42049.
XX
PT   New human fibroblast growth factor protein CX polypeptide, useful for
PT   treating tissue proliferation disorders such as tumors, restenosis,
PT   psoriasis, diabetic complications, Kaposi sarcoma and rheumatoid
PT   arthritis.
XX
PS   Claim 1; Fig 1; 128pp; English.
XX
CC   This invention relates to human fibroblast growth factor-CX (FGF-CX)
CC   the DNA sequence encoding it, FGF-CX protein, and p-lymphocytes
CC   are useful for treating a disease or prevention a disorder associated with aberrant
CC   expression, processing or physiological interactions of FGF-CX
CC   characterised by insufficient or ineffective growth of a cell or tissue.
CC   FGF-CX is also useful for promoting growth of cells which are in the
CC   vicinity of a wound, vascular system, those involved in haematopoiesis or
CC   erythropoiesis, cells in the lining of the gastrointestinal tract, or
CC   cells in hair follicles. Other uses include inhibiting cell growth.
CC   FGF-CX is useful for treating, preventing or delaying a tissue
CC   proliferative disorder such as tumours, restenosis, psoriasis, and
CC   Dupytren's contracture, diabetic complications, Kaposi sarcoma, and
CC   rheumatoid arthritis. Compositions containing FGF-CX can be used to
CC   stimulate cartilage or bone repair. Compositions such as multiple or solitary
CC   binding agents can be used to treat diseases such as achondroplasia, FGF-CX
CC   hereditary exostosis, bony value deformity and cell related disorders,
CC   may be used in diagnosing or treating glial cell related disorders,
CC   central lesions or to treat cerebral oedema, senile dementia,
CC   Alzheimer's disease, or diabetic neuropathy. FGF-CX also has
CC   osteogenesis promoting activity and can be used for treating bone
CC   fractures and osteogenesis. FGF-CX polypeptides may be used as platelet
CC   increasing agents, or for treating cerebral nervous diseases. The present
CC   sequence represents the human FGF-CX protein.
XX
SQ   Sequence: 211 AA;

Query Match   100.0%; Score 1118; DB 22; Length 211;
Best Local Similarity   100.0%; Pred. No.1.6e-111;
Matches   211; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 MAALAVSHLAILALGLMVAAVVGHLTLEFLAKNGAAT-AAGCGLAAQAAHL 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1 maalavsqtlailalglmvaavvghltlefliakrsaatsaaqpaaahl 60

Qy   61 RCLLRRGHLRFLPRSSGWTVGRRRQRFLQTRRWAHLEFLSWAVKVWKRSGHYKS 120
          ||||||||||||||||||||||||||||||||||||||||||||
Db   61 kallrrgylrftahtdlpasqtlftqqtfellqtrrsgvwaslrrgylry 120

Qy   121 MHRKLLTYSSLFLRQHLTBEICLLKHYTVALHKACHTRKCAK 180
          |||||||||||||||||||||||||||||||||||||||||||
Db   121 mhrkllfysslflrqhlts/sgvwasl/kyt/alhkacytrkcak 180

Qy   181 SKEHQKFTHFLPRSVPSRVPSEVEYKRLMYT 211
          |||||||||||||||||||||||||||||||
Db   181 sktqkthflprsvpsrvpseveyqrdllmyt 211

XX
RESULT   4
ID   AAW11548
TD   AAW11548 standard; Protein; 220 AA.
AC   AAW11548;

RESULT 4
AAP27207

ID   AAP27207 standard; protein; 208 AA.
XX
AC   AAP27207;
XX
DT   29-MAY-1998 (first entry)
XX
DE   Glia activating factor #1.
XX
OS   Homo sapiens.
XX
KW   stimulates cultured cells.
KW   osteogenesis promoting activity; osteoporosis, cerebral tumours;
KW   immunocompetent cells; special smooth muscle; bone fractures;
KW   stimulates megakaryocytes; increase platelets; haematopoietic cells;
KW   diabetic neuropathy; stimulates fibroblasts, burns, wounds, ulcers;
KW   cerebral oedema; Alzheimers disease; senile dementia;
CAF: stimulates glial cell growth; cerebral nerve cell lesions;
XX
OS   Homo sapiens.
XX
PN   EP503297-A.
XX
PD   16-SEP-1992.
XX
PF   13-FEB-1992; 92EP-0102385.
XX
PR   14-FEB-1991; 91JP-0020860.
PR   04-SEP-1991; 91JP-0224454.
PR   19-JAN-1992; 92JP-0003499.
XX
PA   (TAKE) TAKEDA CHEM IND LTD.
XX
PI   Kondo T, Kurokawa T, Naruo K, Seko C;
XX
DR   WPI; 1992-409482/38.
DR   N-PSDB; AAQ28411.
XX
PT   Glia activating factor and its DNA, specifically promotes growth
PT   of glial cells, for treating e.g. cerebral lesions, Alzheimer's
PT   disease, diabetic neuropathies, etc., also in diagnosis
XX
PS   Claim 1; Fig 19; 87pp; English.
XX
CC   This sequence represents a glia activating factor. It is expressed
CC   in monkey, G23 7 cells. It stimulates the growth of glial cells and
CC   can be used to accelerate healing of cerebral lesions or treat cerebral
CC   oedema, Alzheimers disease, senile dementia, or diabetic neuropathy. It
CC   also stimulates fibroblasts (for accelerating healing of burns, wounds,
CC   ulcers, etc) megakaryocytes (to increase the no. of platelets),
CC   haematopoietic, immunocompetent and vascular smooth muscle cells. It is
CC   also expected to have osteogenesis-promoting activity (for treating
CC   bone fractures and osteoporosis) Assay of this factor may be useful in
CC   diagnosis of cerebral tumours, and antibodies against it could be used to
CC   treat such tumours. It can also be used as a reagent for stimulating
CC   growth of cultured cells. These can be used for producing...
XX
SQ   Sequence   208 AA;

Query Match   69.3%;   Score 774.5;   DB 13;   Length 208;
Best Local Similarity   70.6%;   Pred. No. 7.8e-75;
Matches 149;   Conservative 23;   Mismatches 40;   Indels 9;   Gaps 4;

Qy   1 MAPLAFWGGRLRGIRESLGQGVGSHP1PPAGFRPPLGERRSAAFRSARG---GRGAAQU 57
            |||||| | | ||||||||||||||||||||||||||||||||||||| | | | |
Db   1 maplgev?qbj.l??qb?--p1agr?cj?   t?p1fl.afb1g50--?ufp?gpavd1 64

Qy   58 AHLHGILFPPPLYCPGEHHQL...P10SVQCFBGHSFPEFHFISVAAF-VSLRGVDSQL 117
            | |||||||||||||||||||||||||| ||||||||||||||||||| ||||||||
Db   55 dhlkali.ra?get?ab?z:r?g?ci?i?q?ct.??i:sfavd?ct:istflffi?bl? 114

Qy   118 YLGMK? t.JLYCSSH.L.LT.ltF.C2TLNNM?V.S:NIYY.v:..???:Y.v.v.v.. 177

RESULT 5

```
Qy   115 ...jnmekqrlyjsekl...........lysse..ph.dcgt;y:dlokdatpte 171
         |||||||||||||||||||  |||||||||   ||  |  :||  :|||||||||||
Db   178 GAYSFRHGKPTHEPLPPPVPVDPEWENFVKDLL 208

Qy   175 qtrkkhgytttlpfrpvdpdkrtqlpkdil 205
         |||||||||||:|||||||||||||||||||
Db   175 qtrkkhgytttlpfrpvdpdkrtqlpkdil 205
```

Db   AAR27215
ID   AAR27215 standard; Protein; 208 AA.
XX
AC   AAR27215;
XX
DT   20-MAY-1998 (first entry)
XX
DE   Glia activating factor #7.
XX
KW   CAF; stimulates glial cell growth; cerebral nerve cell lesions;
KW   cerebral oedema; alzheimers disease; senile dementia;
KW   diabetic neuropathy; stimulates fibroblasts; burns; wounds; ulcers;
KW   stimulates megakaryocytes; increase platelets; haematopoietic cells;
KW   immunocompetent cells; vascular smooth muscle cells; bone fractures;
KW   osteogenesis promoting activity; osteoporosis; cerebral tumours;
KW   stimulates cultured cells.
XX
OS   Homo sapiens.
XX
PN   EP803297-A.
XX
PD   16-SEP-1992.
XX
PF   13-FEB-1992;   92EP-0102385.
PR   14-FEB-1991;   91JP-0020860.
PR   04-SEP-1991;   91JP-0224454.
PR   10-JAN-1992;   92JP-0003355.
XX
PA   (TAKE) TAKEDA CHEM IND LTD.
XX
PI   Kondo I, Kurokawa T, Naruo K, Seko C;
XX
DR   WPI; 1992-309482/38.
XX
PT   Glia activating factor and its DNA. Specifically promotes growth
PT   of glial cells, for treating e.g. cerebral lesions, Alzheimer's
PT   disease, diabetic neuropathies, etc, also in diagnosis.
XX
PS   Claim 1; Pg5; 7pp; English.
XX
CC   This sequence represents a glia activating factor. It stimulates the
CC   growth of glia cells and can be used to accelerate healing of cerebral
CC   lesions or treat cerebral oedema, alzheimers disease, senile dementia,
CC   or diabetic neuropathy. It also stimulates fibroblasts (for accelerating
CC   healing of burns, wounds, ulcers, etc) megakaryocytes (to increase the
CC   no. of platelets), haematopoietic and immunocompetent cells, vascular smooth
CC   muscle cells. It is also expected to have osteogenesis-promoting activity,
CC   (for treating bone fractures and osteoporosis.) Assay of this factor may
CC   be useful in diagnosis of cerebral tumours, and antibodies against could
CC   be used to treat such tumours. It can also be used as a reagent for
CC   stimulating growth of cultured cells. Dosage is 1ug-0.1mg/kg/day.
XX
SQ   Sequence   208 AA;

```
Qy     1 MAPLAEVGGFLSRAYSIGGVVSSHPIIPPAGEPPPLLGEPPSAAFPSAPG---GPCAAQL 57
         |||| ||| |:||:|||:| |   |:||  | |:| |||| ||||| ||      | ||
Db     1 maplaeysyfsgqdav--rpfjm-rplv--dspclsdhlqqse  ddlpirpirtdl 5
```

Query Match   69.3%;   Score 774.5;   DB 13;   Length 208;
Best Local Similarity   70.6%;
Matches   147;   Conservative   23;   Mismatches   30;   Indels   9;   Gaps   4;

RESULT 6

```
Qy    58 AHLHGILPPPQLYCPGTFHLQLLFPGSVGGTRQBHMSLFGILLFISVAAGLVSIRGVDSGL 117
         |:|||||||||||||||||:||||||||||||||||||:|||||||||||||||||||||
Db    58 dhlkgilrrqlycptfhlc:fpqllggttkdhsrfqllelis:awqlsirq:dsql 114

Qy   176 GAYSFRHGKPTHEPLPPPVPVDPEWENFVKDLL 208
         |||||||||||:|||||||||||||||||||||
Db   175 GAYSFRHGKPTHEPLPPPVPVDPEWENFVKDLL 208
```

RESULT 6
Db   AAR56505
ID   AAR56505 standard; peptide; 208 AA.
XX
AC   AAR56505;
XX
DT   06-MAR-1995 (first entry)
XX
DE   Glia activating factor (GAF) peptide.
XX
KW   Glia activating factor, GAF; testing; detection; antibody; cancer;
KW   osteogenesis; platelet; hepatopathy; cirrhosis; anticancer agent.
XX
OS   Homo sapiens.
XX
PN   EP608546-A.
XX
PD   03-AUG-1994.
XX
PF   18-DEC-1993;   93EP-0120491.
PR   22-DEC-1992;   92JP-0342100.
PR   23-AUG-1993;   93JP-0207719.
XX
PA   (TAKE) TAKEDA CHEM IND LTD.
XX
PI   Kurokawa T, Kuroshima K, Seko C, Yoshitomi S;
XX
DR   WPI; 1994-242006/30.
XX
PT   New glia activating factor polypeptide and antibodies for use
PT   in detection, purification and treatment of diseases, e.g. as
PT   anticancer or platelet increasing agents.
XX
PS   Disclosure; Page 40-41; 80pp; English.
XX
CC   The glia activating factor (GAF) polypeptides (See AAR56503-565511) can
CC   be used as platelet increasing agents, osteogenesis promoting
CC   agents or for treating cerebral nervous diseases or hepatopathy, such
CC   as hepatic cirrhosis. They can also be used to treat cancer when
CC   used alongside an anticancer agent. Antibodies directed against the
CC   GAF polypeptides can be used for detecting or determining the
CC   biological activity of a GAF polypeptide or for determining a GAF
CC   polypeptide. The antibodies, which also neutralise the cell growth
CC   activity of GAF, can be used as anticancer agents.
XX
SQ   Sequence   208 AA;

```
Qy     1 MAPLAEVGGFLSRAYSIGGVVSSHPIIPPAGEPPPLLGEPPSAAFPSAPG---GPCAAQL 57
         |||| |||  |:||:|||: | |   |:||  | |:| |||| ||||| ||      | ||
Db     1 AHLHGILRRQLYCPTFHLQLLFPGSVGGTRQBHMSLFGILLFISVAAGLVSIRGVDSGL 117
Db    58 maplaeysyfsgqdav--rpfjm-rplv--dspclsdhlqqse  ddlpirpirtdl 114
```

Query Match   69.3%;   Score 774.5;   DB 15;   Length 208;
Best Local Similarity   70.6%;
Matches   149;   Conservative   23;   Mismatches   36;   Indels   9;   Gaps   4;

RESULT 7

AAR80784

ID   AAR80784 standard; protein; 208 AA.

AC   AAR80784;

DT   14 MAY 1996 (first entry)

DE   Fibroblast growth factor 9, FGF-9.

KW   cell proliferation; regulation; pterygia; corneal clouding; cancer;
KW   psoriasis; rheumatoid arthritis.

OS   Homo sapiens.

PN   WO9524920-A2.

PD   21 SEP 1995.

PF   15 MAR 1995; 95W0-US04448.

PR   15 MAR 1994; 94US-021447.
PR   15 MAR 1994; 94US-021446.

PA   (BAIR/) BAIRD A.

PI   Baird JA; Houston LL; Nova MP; Szabowski BA;

PT   New conjugates of growth factor receptor ligand and targeted agent
PT   - particular fibroblast growth factor, e.g. cytotoxin, saporin, etc.,
PT   used to treat, an FGF-9-specific fusion protein, DNA encoding such fusion
PT   proteins are useful for targeting saporin (a cytotoxin) to a cell
PT   which may be used include in particular DNA encoding a therapeutic protein,
PT   antisense DNA or the cytotoxin saporin. The linked sequence within the
PT   fusion protein may increase serum stability or intracellular
PT   availability of the FGF ... the conjugates of the invention are used to
PT   inhibit cell proliferation in cells carrying the particular growth
PT   factor receptor; also when IA is DNA it can be used to deliver this
PT   to cells (for gene therapy). A specific application is to prevent
PT   excessive proliferation of epithelial cells, fibroblasts and
PT   keratinocytes in the anterior eye after surgery, particle. to prevent
PT   recurrence of pterygia after surgical removal, corneal
PT   trabeculectomy after glaucoma surgery and corneal clouding after
PT   excimer laser treatment, other conditions which may be treated include
PT   tumours, restenosis, psoriasis, Dupuytren's contracture, diabetic
PT   complications, Kaposi's sarcoma and rheumatoid arthritis.

SQ   Sequence 208 AA;

Query Match 69.4%; Score 774.5; DB 16; Length 208;
Best Local Similarity 70.6%;
Matches 147; Conservative ...; Mismatches ...; Indels ...; Gaps ...;

RESULT 8

AAR70822

ID   AAR70822 standard; protein; 208 AA.

AC   AAR70822;

DT   01-SEP-1995 (first entry)

DE   FGF-9.

KW   FGF 9; fibroblast growth factor; cytotoxic conjugate; fusion protein;
KW   saporin; cytostatic; tumor; diabetes; rheumatoid arthritis.

OS   Homo sapiens.

FH   Key   Location/Qualifiers

FT   Misc-difference 68
FT   /note= "gly may be replaced by Ser"

PN   WO9503831-A.

PD   09-FEB-1995.

PF   27-JUL-1994; 94W0-US08051.

PR   02-AUG-1993; 93US-08999924.
PR   29-OCT-1993; 93US-0145829.

PA   (PRIZ/) PRIZM PHARM INC.
PA   (WHIT-) WHITTIER INST DIABETES & ENDOCRINOLOGY.

PI   Baird JA; Lappi DA; Szabowski BA;

PT   New monogenous preparations of cytotoxic conjugates and DNA -
PT   contain fibroblast growth factors and cytotoxic agents for
PT   treating FGF conditions such as tumours, diabetes and rheumatoid
PT   arthritis.

PS   Disclosure; Page 115-116; 128pp; English.

PT   Novel fusion proteins comprise FGF linked to saporin, FGF-1 to -9
PT   may be used, pref. muteins in which at least 1 Cys residue is
PT   replaced by conservative Ser substitutions. The fusion proteins
PT   are potent cytocidal agents to cells bearing the FGF receptor.

SQ   Sequence 208 AA;

Query Match 69.4%; Score 774.5; DB 16; Length 208;
Best Local Similarity 70.6%; Pred. No. 7.8e-75;
Matches 147; Conservative 23; Mismatches 40; Indels 9; Gaps 4;

RESULT 9

ID   AAW1547
AC   AAW1547;
XX
DT   17-SEP-1997 (first entry)
XX
DE   Amino acid sequence of mouse FGF9 encoded by FGF9-pET-3c.
XX
KW   Mouse; chicken; fibroblast growth factor 9; FGF9; detection;
KW   fibroblast growth factor receptor 3; FGFR3; cartilage repair;
KW   bone repair; antagonist; anti-FGF9 antibody; endochondroma;
KW   solitary hereditary exostosis; multiple hereditary exostosis;
KW   hallux valgus deformity; achondroplasia; synovial chondromatosis.
XX
OS   Mus musculus.
XX
PN   WO9641523-A1.
XX
PD   27-DEC-1996.
XX
PF   12-JUN-1996; 96WO-US0011.
XX
PR   12-JUN-1995; 95US-0000137.
XX
PA   (YEDA) YEDA RES & DEV CO LTD.
XX
PI   Yayon A;
XX
DR   WPI; 1997-065215/06.
DR   N-PSDB; AAT58530.
XX
PT   Medical and diagnostic use of fibroblast growth factor 9 - and
PT   recombinant fibroblast growth factor 9 DNA.
PS   Claim 12; Fig 1; 32pp; English.
XX
CC   The sequences given in AAW1547-48 represent mouse and chicken
CC   fibroblast growth factor 9 (FGF9) respectively. FGF9 may be used in the
CC   method of the invention for detecting fibroblast growth factor receptor 3
CC   (FGFR3) in a sample or tissue. The method comprises contacting the
CC   sample or tissue with FGF9, allowing formation of receptor-ligand pairs,
CC   and detecting any FGFR3-FGF9 pairs. Compositions containing FGF9 can
CC   be used to increase FGFR3 activity, esp. to stimulate cartilage or bone
CC   repair. Compositions containing FGF9 antagonists or FGF9 binding agents
CC   (e.g. anti-FGF9 antibodies) can be used to treat diseases caused by an
CC   excess of FGF9 or overactivity of FGFR3, esp. multiple or solitary
CC   hereditary exostosis, hallux valgus deformity, achondroplasia, synovial
CC   chondromatosis and endochondromas.
XX
SQ   Sequence 208 AA;

Query Match   69.4%; Score 774.5; DB 18; Length 208;
Best Local Similarity   70.6%;
Matches 147 Conservative   23; Mismatches   40; Indels   5; Caps   1;

RESULT 10

ID   AAW75719
AC   AAW75719;
XX
DT   07-DEC-1998 (first entry)
XX
DE   Fibroblast growth factor-9.
XX
KW   Fibroblast growth factor-9; FGF-9; mutein; protein engineering;
KW   heparin; thrombosis; thrombocytopenia; ophthalmic disorder;
KW   human; therapy.
XX
OS   Homo sapiens.
XX
FH   Key   Location/Qualifiers
FH
FT   Misc-difference 136
FT   /note= "Phe-136 is replaced by another amino
FT   acid (claim 3), preferably Ala, Phe, Ser,
FT   Gly, Met, Leu or Tyr, especially Ala, Gly
FT   or Ser"
FT   Misc difference 137
FT   /note= "Glu-137 may be replaced by another amino
FT   acid (claim 7), preferably Ala, Gly or Ser"
FT   Misc-difference 143
FT   /note= "Asn-143 may be replaced by another amino
FT   acid (claim 2), preferably Ala, Phe, Ser,
FT   Gly, Met, Leu or Tyr, especially Ala, Gly
FT   or Ser"
FT   Misc-difference 146
FT   /note= "Asn 146 may be replaced by another amino
FT   acid (claim 1), preferably Ala, Phe, Ser,
FT   Gly, Met, Leu or Tyr, especially Ala, Gly
FT   or Ser"
XX
PN   WO9836436-A2.
XX
PD   11-SEP-1998.
XX
PF   03-MAR-1998; 98WO-JP00878.
XX
PR   03-MAR-1997; 97US-0040785.
XX
PA   (EISA) EISAI CO LTD.
XX
PI   Kuriyama K; Kawai T; Zhu H;
XX
DR   WPI; 1998-495843/42.
XX
PT   Fibroblast growth factor mutein and DNA - having reduced receptor
PT   binding and able to bind heparin, useful for treating and regulating
PT   heparin-related disorders e.g. thrombosis.
XX
FS   bio.source, Page 59-60; /lpp; English.

XX
CC   This is the amino acid sequence of fibroblast growth factor-9
CC   (FGF-9). Claimed DNA molecules of the invention encode FGF protein
CC   polypeptides (see AAW75711 20) that show reduced FGF receptor binding
CC   activity but which retain the ability to bind heparin. For FGF-9,
CC   amino acid residues 136, 143 and 146 are preferably replaced by
CC   other amino acid residues, with an optional further replacement of
CC   the Cys 147 residue. The protein may be further modified by
CC   replacement of the Cys residues to reduce aggregation. The mutein
CC   is obtained by site-specific or site directed mutagenesis of the
CC   DNA incorporated into a vector and expression
CC   in host cells. The FGF muteins are used to treat heparin-related
CC   disorders, such as excessive fibrinolysis induced by heparin,
CC   ophthalmic disorders and heparin-associated thrombocytopenia and
CC   thrombosis. They may also be used for drug design.
XX
SQ   Sequence   208 AA;

Query Match   65.8%; Score 771.5; DB 14; Length 208;
Best Local Similarity   70.6%; Pred. No. 7.8e-75;
Matches 149; Conservative   24; Mismatches   30; Indels   9; Gaps 4;

[sequence alignment block — illegible]

PS   Disclosure; Page 52; 94pp; English.
XX
CC   Fibroblast growth factor (FGF) proteins (AAW5022-W5024;W5024 and
CC   AAW5025;W50415) are members of the fibroblast growth factor family
CC   have homology to fibroblast growth factor homologous factor (FHF)
CC   proteins. The FHF proteins (FHF 1-4) are involved in regulating the
CC   growth, survival, and differentiation of cells in the central nervous
CC   system, as well as cells in peripheral nervous tissues, the proteins can
CC   therefore be used for treating and diagnosing conditions involving the
CC   nervous system. FHF's can also be used in methods for maintaining
CC   cultured cells or tissues or to promote neuron growth in vitro.
XX
SQ   Sequence   208 AA;

Query Match   65.8%; Score 771.5; DB 14; Length 208;
Best Local Similarity   70.6%; Pred. No. 7.8e-75;
Matches 149; Conservative   24; Mismatches   30; Indels   9; Gaps 4;

[sequence alignment block — illegible]

Left column:

```
XX
DE   FGF-9, Seq ID No.18.
XX
KW   targeted gene delivery; therapeutic; nucleic acid; receptor;
KW   FGFR-binding protein; FGF-2; nucleic acid binding protein;
KW   receptor-internalized ligand; receptor; acidic; FGF; b
KW   cytotoxic; antiproliferative; cancer; melanoma; diabetic retinopathy;
KW   rheumatoid arthritis; restenosis; Dupuytren's contracture; psoriasis;
KW   eczema.
XX
OS   Unidentified.
XX
YY
OS   US60187429-A.
KW
XX
PD   14 MAR 2000.
XX
PF   24 SEP 1996;  9608-07189304.
XX
PR   15 MAR 1994;  94US-0218446.
PR   15 MAR 1994;  94US-0218447.
PR   29 AUG 1994;  94US-0297961.
PR   13 SEP 1994;  94US-0305771.
PR   16 MAY 1995;  95US-0441979.
XX
PA   (SELE ) SELECTIVE GENETICS INC.
XX
PI   Chandler LA, Sosnowski BA, Baird A.
XX
WPI  2000-292008/25.
XX
PI   Gene delivery system, useful for treating or preventing cancer and
PI   rheumatoid arthritis, comprises receptor-internalized ligand linked to
PI   nucleic acid binding domain and nucleic acid -
XX
PS   Claim 25; Columns 107-110; 141pp; English.
XX
CC   The invention relates to a novel gene delivery composition for the
CC   targeted delivery of genes to proliferating cells. The gene delivery
CC   proliferating cells. The gene delivery composition comprises a protein
CC   that binds the fibroblast growth factor receptor (FGFR) which is fused
CC   or chemically conjugated to a nucleic acid binding domain. The nucleic
CC   acid binding domain is complexed with a suitable expression construct
CC   encoding a cytotoxin such as saporin. One or more linkers may join the
CC   FGFR-binding proteins to the nucleic acid binding protein. These are
CC   selected to increase the specificity, toxicity, solubility, serum
CC   stability or intracellular availability, and may serve to decrease the
CC   condensation of nucleic acids for delivery to a cell. The fusion protein
CC   binds to FGFR and is internalized by cells that carry this receptor. The
CC   gene delivery composition is used for the therapeutic alteration of the
CC   function, gene expression, and viability of cells. In particular, it may
CC   be used for the treatment and prevention of cell proliferative
CC   disorders, for example after eye surgery, melanoma and many other sorts
CC   of cancer, rheumatoid arthritis, restenosis, Dupuytren's contracture,
CC   diabetic retinopathy, psoriasis and eczema. The gene delivery
CC   compositions of the invention have high specificity for FGF receptor cells
CC   and can deliver large amounts of DNA compared to prior art methods.
CC   Sequences AAY90410-AAY90418 represent members of the fibroblast growth
CC   factor (FGF) family of proteins. AAY90419P represents wild type human
CC   FGF 2 (basic FGF, bFGF) which is encoded by AAA72868, AAA72897 A12903
CC   encode the human FGF-2 muteins AAY90464, and AAY90465-Y90466
CC   represent additional human FGF-2 muteins used in the invention. AAY90456
CC   represents a mutated human FGF C-terminus.
XX
SQ   Sequence;   208 AA;
```

```
QY   Query Match            69.4%;  Score 174.5;  DB 25; Length 209;
       best local Similarity   76.6%;  Pred No. 7 to 75;
       Matches 14;  Conservative 3;  Mismatches 4;  Indels 9;  Gaps 1;

QY    1 MAPLAEV...
         ||||| :| :| | : :||   ||    |    | :|  ||     || :|
Db    1 MAPLQE...
```

Right column:

```
QY   58 AnLHG...LRKGVRK...ISVGGSVRQHSL...ISVAVGV.VS IKVNPSGL 117
         ||||||||| :|||||   |   |||:| ||||||||||   |:|| ||||||
Sb    ...........................................................  177
XX
QY  175 CARS...FTHFLPGNDVDERVFVFLRVVEPII 208
         ||| |  | |:|| | |||| |:| |:||||
Sb  175 ...........................  205
```

```
RESULT  15
ID   AAY32341 standard; protein; 208 AA.
XX
AC   AAY32341;
XX
DT   28-FEB-2000  (first entry)
XX
DE   Human fibroblast growth factor 9.
XX
KW   fibroblast growth factor 9; FGF-9; human; mutein;
KW   vascular disorder; smooth muscle cell proliferation;
KW   rheumatoid arthritis; tumour; atherosclerosis; Kaposi's sarcoma;
KW   restenosis; ophthalmic disorder; psoriasis; coagulant; heparin;
KW   thrombosis; thrombocytopenia.
XX
OS   Homo sapiens.
XX
FH   Key      Location/Qualifiers
FH
FT   Misc-difference  186
FT                    /note "replaced with another amino acid in
FT                    claimed mutein of Claim 1"
FT   Misc-difference  130
FT                    /note "replaced with another amino acid in
FT                    claimed mutein of Claim 5"
FT   Misc-difference  135
FT                    /note "replaced with another amino acid in
FT                    claimed mutein of Claim 7"
XX
PN   WO9955861-A2.
XX
PD   04 NOV-1999.
XX
PF   15 APR 1999,  98WO-JP02013.
XX
PR   28-APR-1998;  9898-JUK7929.
XX
PA   (EISA ) EISAI CO LTD.
XX
PI   Zhu H, Kalyanaraman R;
XX
WPI  2000-062346/05.
XX
PS   Claim 1; Page 85; 93pp; English.
XX
CC   This sequence represents human fibroblast growth factor 9 (FGF-9).
CC   The invention relates to isolated nucleic acids encoding FGF mutein
CC   polypeptides. FGF muteins that exhibit increased binding affinity
CC   for FGF receptors and reduced mitogenic activity are provided. Such
CC   muteins have amino acid replacements at positions corresponding to
CC   positions 138 (Claim 1) of FGF 2 (see AAY32341). They can be used to
CC   prevent or inhibit the undesired growth and proliferation of
CC   FGF responsive cells. Such cells occur in vascular disorders
CC   characterised by accelerated smooth muscle cell proliferation, such
CC   as rheumatoid arthritis, tumour angiogenesis, Kaposi's sarcoma,
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restenosis, in-stent restenosis, certain ophthalmic disorders and
dermatological disorders, such as psoriasis. Also provided are
FGF muteins that exhibit reduced receptor binding activity, but
retain the ability to bind heparin. These muteins have amino acid
replacements corresponding to positions 88 (claim 5) and 94 (claim
7) and optionally position 96 of FGF-2. They can be used as
antagonists for heparin associated bleeding, antagonists of
heparin-induced angiogenesis, and for treating heparin-induced
thrombocytopenia and thrombosis. In preferred muteins, the native
FGF amino acid is replaced by Ala, Phe, Gly, Ser, Met or Tyr,
especially Ala, Gly or Ser, and particularly Ala. Cys residues
may also be substituted to reduced polypeptide aggregation.

XX
SQ   Sequence   208 AA;

Query Match   69.9%; Score 774.5; 99.2%; Length 208;
Best Local Similarity   70.6%; Pred. No. 7.8e-75;
Matches 149; Conservative 23; Mismatches 40; Indels 9; Gaps 4;

Qy   1 MAPLAEVGG...   57
Db   1 map...   54

Qy   58 AHLRG...   117
Db   55 ddlk...   114

Qy   118 LLPE...   177
Db   115 ylann...   174

Qy   178 CAPPR...   208
Db   175 wttk...   205